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HOMEOCHRONOUS HEREDITARY OPTIC-NERVE ATROPHY, EXTENDING THROUGH SIX GENERATIONS.

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HOMEOCHRONOUS[1] HEREDITARY OPTIC-NERVE ATROPHY, EXTENDING THROUGH SIX GENERATIONS.*

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THE cases I herewith report are in several aspects unique, and in their suggestions and inferences are of most abundant interest. The diagram annexed shows fourteen or more instances of hereditary optic atrophy scattered through six generations. The details will be made clear under the general aspects considered as follows:

Pathogeny and Pathology. The earliest ancestor in whom, so far as ascertainable, the affliction appeared, was a sea captain. All that I can learn about him is that he became blind and deaf somewhat late in life. His two sons became blind "from the same type of disease as that which has since appeared in the later generations." The hereditary nature of the affection is certain from the first generation downward. The primary cause, so far as I can see, is involved in complete mystery. The disease seems to be typical white atrophy of the optic nerve. In my patient the failure of vision was first noticed in March, 1892, and in nine months progressed to barely counting fingers. I have been able

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[1] ὁμοιος, similar; χρόνος, time. Applied to a hereditary trait or disease, appearing at a similar age or time of life in a line of descendants.

to get reports from hospitals, and other oculists who have examined other members of the family affected, and they all agree in the diagnosis.[2]

Macula-vision is not so good in my patient as vision with a more peripheral portion of the retina. In a number of the cases the blindness is not absolute, but the patients have some slight vision that is retained through life.

The Influence of Sex in Transmitting the Malady is most marked and peculiar. In the entire series of histories there is not a pure or idiopathic instance of the appearance of the disease in a woman. In the third generation No. 3 had "weak eyes," and persistent "watering" of the eyes, but she was not blind. Her sister, No. 4, became blind before her death (at 40), but she was "horned in the temple by a cow and one eye thus destroyed," blindness following in the other eye a few months later. The remaining sister, No. 5, became blind late in life, from what cause I am unable to say. As none of her children were affected I am inclined to think the cause must have been cataract and not optic atrophy.

But the most interesting phase of this subject consists in the remarkable fact that after the second generation no man transmits the affection to his descendants, and it is always transmitted by women who are unaffected. Passing the line through a male, even though he himself is blind with the disease, at once stops the appearance of the disease. In this respect a similar law obtains in the hereditary transmission of hemophilia, which is often or largely through unaffected females. The same peculiarity has also been observed in idiopathic muscular atrophy, and I think cases of color-blindness have also been reported.

It is most noteworthy that in one group of my cases the inheritance is consecutively transmitted through two unaffected females, and in another group it is passed through three women.

There is one seeming or partial exception to the last law: In the fourth generation one man has a blind son, No. 4, who still lives at the age of 52. "While chipping something, a small piece flew in the eye; the injury was slight, but blindness resulted. The other eye is now partially blind and failing." This incident together with others and especially the histories of the three sisters in the third generation, show that normal vision or ocular health in the family was always on a precarious equilibrium, and when

[2] I am greatly indebted to Rev. T. M. Jackson, of Norristown, Pa., for his patient and scientific labor in gathering the details of the cases reported.

optic atrophy did not arise idiopathically, only a slight accident or exciting circumstance was needed to bring on a train of evil results.

Ingravescence of the Affection in later Generations. According to *a priori* expectation, and also according to other histories and hereditary laws, we should expect the disease to decrease in virulence with each intermixture of new blood, or with each marriage. But in the diagram we note that in the fourth generation there is but one example, while in the fifth there are six or seven. In the fifth generation there is but one woman who became a mother, and of her children I shall speak by and by. It seems clear that if there had been more mothers in the fifth generation there would have been a sad increase of blind men in the sixth generation. Did "Nature" with subtle wisdom prevent this? It would also seem that the age at which the affliction appears is earlier with later generations.

If not Optic-Atrophy, Death. The proportion of early deaths has struck my attention. This begins to become manifest in the fourth generation. In the children of III-3, there are four deaths in infancy; in those of III-5, there are three, and besides three or four deaths in early adult life—at about the age the optic atrophy appears in others. In the fifth generation, all the males that live in one family are afflicted with blindness in early adult life, and the four other males born die in infancy. This virulence is to be connected with the fact that the line comes through a female. In the children of the second family the line passes through a male, and while the law is greatly modified, its power is shown by one death in infancy, and others at 28, 30, 35, 40, 46, and 48, with one case of blindness secondarily induced. In another family of this generation two males died in infancy, only one son surviving; in another, two sons die in early manhood, etc. The fathers of these transmit the line; but in the last case to be cited, a mother is the medium, and of her four sons, one dies in infancy and the other three are struck with blindness at 23, 28, and 34, respectively.

In the sixth generation, the only children who have a mother in this ancestral line are thus endowed:—three die in infancy; one, a girl, has a "weak mind;" one has optic atrophy at 27, and two younger brothers have chronically abnormal eye-grounds and optic-nerve heads.

Finally, it is suggestive to see that this law of extinction is probably now complete, or about to end. If my reading of the facts

is correct, i. e., if only the female transmits the tragic inheritance, and only to males, there will, so far as I can learn, be no further cases, except possibly in the brothers of my patient VI-5. Every female child of a female of the line is now dead or childless. After discovering this law I was greatly anxious to see the brothers of my patient. With much difficulty I at last succeeded. My little scientific pleasure was immeasurably overbalanced by the sad ophthalmoscopic findings: in both there was a retina congested, stippled, and with chronic degenerative changes taking place, an optic nerve unhealthy, without clear outlines, and hyperemic—altogether a morbid fundus—though the young men have so far had no visual trouble. I shall watch the approach of the ominous age with much interest.

There still remains to note the great predominance of males in the later generations, a factor that tends to bring the vicious inheritance to a sharp ending. But the same purpose is outworked, and more manifestly, by the rapid decrease of prolific females whose ancestral line decends through women unbroken by a male of the line. In the third generation, when the vicious tendency becomes manifest, there are two child-bearing females, a percentage to all children born of sixty-six and two-thirds. In the fourth generation the percentage is less than three, and in the sixth generation it is brought to zero. There is now no existing female, except one mentally weak and childless, who has had uninterrupted female ancestors of the line back to the second generation.

Homeochronicity. Habershorn (*Transac. Oph. Soc. Unit. King., 1888*) gives a complete review of the literature of hereditary optic atrophy up to the time he wrote. In the great majority of the cases he reviews, the ages at which the onset of the disease occurred fall between 15 and 19. In both sexes, the cases more or less roughly group themselves about the period of puberty, and that approximating 40. The cases I report decidedly neutralize this law, if such it may be termed, and throw the subject back into the mystery from which it seemed emerging. In the first three or four generations there was some approximation toward grouping about the age of 40, but in the last two generations the onset of the disease more clearly and decidedly clusters about the ages of full adult vigor,—i. e., from 23 to 34.

or circles, for conspicuousness; black border, cases of hereditary optic atrophy; Roman numerals at side, the generation; small numerals above figures, children of the generation. Numerals in squares: *a*, if in black-bordered figure, age at which atrophy appeared; *b.*, if with "D.," date of death; *c.*, if alone, present age of patient; D. I., died in infancy; large squares or circles, with outline borders, are explained in the text.